reporter being optically distinguished by said specific imaging system in response to an optical characteristic of the aggregate reporter other than size and shape.--

REMARKS

Status of the Claims

Claims 1-40 are now pending in the present application, new Claims 8-40 having been added and Claims 3 and 6 having been amended by the present preliminary amendment. A Supplemental Combined Declaration and Power of Attorney, executed by the inventors in this application, is submitted concurrently herewith.

The Examiner is requested to consider the application in the light of the above preliminary amendment. In the event that any issues arise during the course of such consideration, the Examiner is invited to telephone applicants' attorney at the number listed below.

Respectfully submitted,

Ron Anderson

Ronald M. Anderson
Registration No. 28,829

I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed envelope as first class mail with postage thereon fully prepaid addressed to: Director of Patents and Trademarks, Arlington, VA 22202 on June 25, 2002.

Kathy Perkins

Date: June 25, 2002

RMA:MCK:klp

Enclosure
Supplemental Combined Declaration and Power of Attorney

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

MARKED-UP VERSION OF THE AMENDMENTS

Amendment to the Claims

In the Claims:

Please amend Claims 3 and 6 as follows:

3. (Amended) A method of constructing a library of uniquely identifiable reporters [labeled carriers] suitable for labeling beads to be used to generate a bead library, said method comprising the steps of:

(a) providing a plurality of singly labeled micro-particles, each singly labeled micro-particle comprising a uniquely identifiable characteristic;

(b) determining a number of unique reporters required to completely encode a desired bead library, based on the uniquely identifiable characteristics of said plurality of singly labeled micro-particles;

(c) providing a plurality of separate reaction vessels, including one reaction vessel for each unique reporter signature required;

(d) apportioning said singly labeled micro-particles among the plurality of reaction vessels, such that each reaction vessel contains at least one singly labeled micro-particle required to generate a unique reporter signature associated with that reaction vessel;

(e) for each reaction vessel requiring additional singly labeled micro-particles to generate a unique reporter signature associated with that reaction vessel, adding appropriate singly labeled micro-particles having a complementary chemistry until substantially all singly labeled micro-particles in that reaction vessel have combined;

(f) repeating step (e) in a stepwise fashion until each reaction vessel contains either a singly labeled micro-particle having a unique reporter signature associated with that reaction vessel, or a combination of singly labeled micro-particles having a unique reporter signature associated therewith.

6. (Amended) The method of Claim 3, further comprising the step of [using a contents of] introducing a plurality of beads into each reaction vessel to [combinatorially] generate said desired labeled bead library under conditions favorable to allowing substantially all singly labeled micro-particle or combinations of singly labeled micro-particles in the reaction vessels to attach to the plurality of beads, to produce a plurality of reporter labeled beads.

Please add new Claims 8-40 as follows:

--8. A method of constructing a library of optically distinct reporter labeled carriers, said method comprising the steps of:

(a) providing a plurality of optically distinct carriers;

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

(b) providing a plurality of reaction vessels, such that at least one reaction vessel is available for each unique member of the library to be constructed;

(c) providing a plurality of optically distinct reporters;

(d) in each reaction vessel, apportioning at least one carrier and at least one reporter in a predetermined unique combination; and

(e) attaching said at least one reporter to said at least one carrier in each reaction vessel, by at least one of a physical attachment and a chemical attachment.

9. The method of Claim 8, wherein no reaction vessel contains a mixture of different optically distinct carriers.

10. The method of Claim 8, wherein said plurality of optically distinct reporters and said plurality of optically distinct carriers are optically distinguishable based on size.

11. The method of Claim 8, wherein said plurality of optically distinct reporters and said plurality of optically distinct carriers are optically distinguishable based on intensity.

12. The method of Claim 8, wherein said plurality of optically distinct reporters and said plurality of optically distinct carriers are optically distinguishable based on shape.

13. A method of constructing an optically discriminable reporter that is distinguishable by a specific imaging system used to optically distinguish said optically discriminable reporter, comprising the steps of:

(a) providing a plurality of singly labeled microparticles, each singly labeled microparticle having a uniquely identifiable optical characteristic, each singly labeled microparticle being smaller than a resolution limit of said specific imaging system employed to optically distinguish said optically discriminable reporter; and

(b) combining a plurality of said singly labeled microparticles together to generate an aggregate reporter having a size larger than said resolution limit, to enable the aggregate reporter to be optically distinguished by said specific imaging system.

14. The method of Claim 13, wherein each singly labeled microparticle comprises one of a quantum dot and a micro-bead.

15. The method of Claim 13, wherein the uniquely identifiable characteristic comprises a color.

16. The method of Claim 13, wherein the uniquely identifiable characteristic comprises an intensity.

17. The method of Claim 13, wherein each of the plurality of singly labeled microparticles comprising said aggregate reporter comprises has an identical uniquely identifiable characteristic.

18. The method of Claim 13, wherein said aggregate reporter comprises at least two groups of singly labeled microparticles each group having a different uniquely identifiable characteristic.

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

19. A method of constructing a plurality of reporters comprising the steps of:

(a) providing a plurality of singly labeled microparticles that individually are incapable of functioning as reporters, each singly labeled microparticle having a uniquely identifiable characteristic, each singly labeled microparticle being smaller than a resolution limit of an imaging system that is to be employed to optically distinguish said plurality of reporters;

(b) determining a number of unique reporters desired, each unique reporter being indicated by the uniquely identifiable characteristics of said plurality of singly labeled microparticles;

(c) providing a plurality of separate reaction vessels, such that a different separate reaction vessel is provided for each unique reporter desired, each separate reaction vessel being associated with a different unique reporter;

(d) apportioning said singly labeled microparticles among the plurality of reaction vessels, such that each reaction vessel contains at least one of each singly labeled microparticle required to generate a unique reporter signature associated with that reaction vessel;

(e) for each reaction vessel other singly labeled microparticles to generate the unique reporter signature associated with that reaction vessel, adding the other singly labeled microparticles until substantially all singly labeled microparticles in that reaction vessel have combined; and

(f) repeating step (e) in a stepwise fashion until each reaction vessel contains an aggregate of singly labeled microparticle defining the unique reporter signature associated with that reaction vessel.

20. The method of Claim 19, wherein each singly labeled microparticle comprises one of a quantum dot and a micro-bead.

21. The method of Claim 19, wherein the uniquely identifiable characteristic is a color.

22. The method of Claim 19, wherein the uniquely identifiable characteristic is an intensity.

23. The method of Claim 19, wherein the uniquely identifiable characteristic is a shape.

24. A method of preparing a library of diverse compounds, each compound including a plurality of components and being produced by a combination of a directed synthesis and a combinatory synthesis, said method comprising the steps of:

(a) providing a plurality of optically distinct carriers;

(b) providing a plurality of reaction vessels, such that a different reaction vessel is available for each different type of optically distinct carrier;

(c) apportioning said plurality of optically distinct carriers among said plurality of reaction vessels, such that each reaction vessel contains only one type of optically distinct carrier;

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

(d) in each of said plurality of reaction vessels, performing a directed synthesis by exposing said optically distinct carriers to a plurality of first components until substantially all optically distinct carriers have coupled to at least one first component, a different first component being added to each reaction vessel, such that each type of optically distinct carrier identifies a different first component;

(e) pooling contents from each reaction vessel, to form a common pool comprising said plurality of optically distinct carriers;

(f) apportioning the common pool among said plurality of reaction vessels, such that each reaction vessel contains a mixture of different optically distinct carriers and first components;

(g) in each reaction vessel, exposing each mixture to a plurality of optically distinct first reporters, until substantially all optically distinct carriers have at least one optically distinct first reporter coupled thereto, a different optically distinct first reporter being added to each reaction vessel; and

(h) performing a combinatory synthesis by exposing each mixture of different optically distinct carriers, different first components, and different optically distinct first reporters in each reaction vessel to a plurality of second components, until substantially all optically distinct carriers have at least one second component coupled thereto, a different second component being added to each reaction vessel, such that each different optically distinct first reporter identifies a different second component.

25. The method of Claim 24, wherein after the step of exposing each mixture of different optically distinct carriers, different first components and different optically distinct first reporters to a plurality of second first components, further comprising the steps of:

(a) pooling the contents of each reaction vessel to form a second common pool;

(b) apportioning said second pool among said plurality of reaction vessels, such that each reaction vessel contains a second mixture of different optically distinct carriers, first components, optically distinct first reporters, and second components;

(c) in each reaction vessel of said plurality of reaction vessels, exposing each second mixture of different optically distinct carriers, first components, first reporters, and second components to a plurality of optically distinct second reporters, until substantially all optically distinct carriers have at least one optically distinct second reporter coupled thereto, a different second optically distinct reporter being added to each reaction vessel; and

(d) performing a combinatory synthesis by exposing each second mixture of different optically distinct carriers, first components, optically distinct first reporters, second components, and optically distinct second reporters to a plurality of third components, until

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

substantially all optically distinct carriers have at least one third component coupled thereto, a different third component being added to each different reaction vessel, such that each type of optically distinct second reporter identifies a different third component.

26. The method of Claim 25, further comprising the step of repeating the steps of pooling, apportioning, exposing to a different reporter, and exposing to a different component, as in Claim 25, until a desired number of components have been added to said plurality of optically distinct carriers.

27. The method of Claim 24, wherein said plurality of optically distinct carriers are optically distinguishable based on size.

28. The method of Claim 24, wherein said plurality of optically distinct carriers are optically distinguishable based on intensity.

29. The method of Claim 24, wherein said plurality of optically distinct carriers are optically distinguishable based on shape.

30. The method of Claim 24, wherein each different optically distinct reporter is optically distinguishable based on size.

31. The method of Claim 24, wherein each different optically distinct reporter is optically distinguishable based on light intensity.

32. The method of Claim 24, wherein each different optically distinct reporter is optically distinguishable based on shape.

33. The method of Claim 24, wherein after the step of exposing each mixture of different optically distinct carriers, different first components and different optically distinct first reporters to a plurality of second components, further comprising the steps of:

(a) pooling the contents of each reaction vessel to form a second common pool;

(b) apportioning said common pool among less than all of said plurality of reaction vessels, such that at least one reaction vessel remains empty, and that a remainder of the plurality of reaction vessels each contains the mixture of different optically distinct carriers, first components, first optically distinct reporters, and second components;

(c) in each of the remainder of reaction vessels, exposing each mixture of different optically distinct carriers, first components, first optically distinct reporters, and second components to a plurality of optically distinct second reporters, until substantially all optically distinct carriers are coupled to at least one optically distinct second reporter, a different second reporter being added to each of the remainder of the reaction vessel; and

(d) performing a constrained combinatory synthesis in each of the remainder of the reaction vessels by exposing each mixture of different optically distinct carriers, first components, first optically distinct reporters, second components and second optically distinct reporters to a plurality of third components, until substantially all optically distinct carriers are coupled to at least one third

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

component, a different third component being added to each of the remainder of the reaction vessels, such that each type of optically distinct second reporter identifies a different third component.

34. A method of preparing a library of diverse compounds by a step-wise synthesis, each compound including a plurality of components, comprising the steps of:

(a) providing a plurality of reaction vessels, such that a different reaction vessel is provided for each different compound to be prepared;

(b) providing a plurality of optically distinct carriers of different types, fewer different types of optically distinct carriers being provided than a number of the reaction vessels that are provided;

(c) apportioning said plurality of optically distinct carriers among said plurality of reaction vessels, such that at least two reaction vessels contain an identical type of optically distinct carrier;

(d) in each reaction vessel of said plurality of reaction vessels, exposing said optically distinct carriers to a plurality of first components, until substantially all optically distinct carriers have at least one first component coupled thereto, identical first components being added to each reaction vessel that contains the identical type of optically distinct carrier; and

(e) in each reaction vessel of said plurality of reaction vessels, exposing said optically distinct carriers to a plurality of second components, until substantially all optically distinct carriers coupled to at least one second component, identical second components being added to each reaction vessel that contains the identical type of optically distinct carrier, such that each different type of optically distinct carrier uniquely identifies a specific combination of first and second components.

35. The method of Claim 34, wherein after the step of exposing said optically distinct carriers to a plurality of second components, further comprising the steps of:

(a) in each reaction vessel, exposing said optically distinct carriers to a plurality of third components, until substantially all optically distinct carriers are coupled to at least one third component, different types of third components being added to each reaction vessel that contains the identical type of optically distinct carrier; and

(b) in each reaction vessel, exposing said optically distinct carriers to a plurality of optically distinct first reporters, until substantially all optically distinct carriers are coupled to at least one first optically distinct first reporter, an identical optically distinct first reporter being added to each reaction vessel containing the same third component, such that each type of optically distinct first reporter identifies a different third component.

36. The method of Claim 35, wherein in each reaction vessel, after the step of exposing said optically distinct carriers to a plurality of optically distinct first reporters, further comprising the

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

step of exposing said optically distinct carriers to a plurality of fourth components, until substantially all optically distinct carriers are coupled to have at least one fourth component, the identical type of fourth component being added to each reaction vessel, such that each type of optically distinct first reporter uniquely identifies a specific combination of third and fourth components.

37. A method of preparing a library of different compounds by a step-wise synthesis, each compound including at least one component and being uniquely identified by a plurality of optically distinct reporters, said plurality of optically distinct reporters being added in a single portion of said step-wise synthesis, said method comprising the steps of:

(a) providing a plurality of carriers;

(b) providing a plurality of reaction vessels, such that a separate reaction vessel is provided for each different compound to be prepared;

(c) providing a plurality of optically distinct reporters of different types, such that a sufficient number of different types of optically distinct reporters are provided so as to enable each different compound to be prepared to be uniquely identifiable using a unique combination of optically distinct reporters;

(d) apportioning said plurality of carriers among said plurality of reaction vessels;

(e) in each reaction vessel, exposing said plurality of carriers contained therein to a different combination of optically distinct reporters, until substantially all carriers are coupled to at least one combination of optically distinct reporters, carriers in different reaction vessels thus exposed having different optical signatures, due to the different combination of optically distinct reporters; and

(f) in each reaction vessel, exposing said plurality of carriers to a plurality of first components, until substantially all of the plurality of carriers are coupled to at least one first component.

38. The method of Claim 37, wherein for each reaction vessel that was provided for a compound that requires at least another component, further comprising the step of exposing said plurality of carriers to any other components thus required, in a step-wise fashion, until each reaction vessel contains the compound for which the reaction vessel was provided.

39. A method of preparing a library of different compounds by a step-wise synthesis, each different compound being uniquely identified by a plurality of optically distinct reporters, said method comprising the steps of:

(a) providing a plurality of carriers;

(b) providing a plurality of reaction vessels, such that a separate reaction vessel is provided for each different compound to be prepared;

(c) providing a plurality of optically distinct reporters of different types, such that a sufficient number of different types of optically distinct reporters are provided so as to enable each

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

different compound to be prepared to be uniquely identifiable using a unique combination of optically distinct reporters;

(d) apportioning said plurality of carriers among said plurality of reaction vessels;

(e) in each reaction vessel of said plurality of reaction vessels, exposing said plurality of carriers to a different combination of optically distinct reporters, until substantially all of the plurality of carriers are coupled to at least one combination of optically distinct reporters, carriers from different reaction vessels comprising different optical signatures, due to the different combination of optically distinct reporters added to each reaction vessel; and

(f) in each reaction vessel, exposing said plurality of carriers to a plurality of compounds, until substantially all of the plurality of carriers are coupled to at least one compound coupled, a different compound being added to each reaction vessel.

40. A method of constructing an optically discriminable reporter that is distinguishable by a specific imaging system used to optically distinguish said optically discriminable reporter, comprising the steps of:

(a) providing a plurality of singly labeled microparticles, each singly labeled microparticle having a uniquely identifiable optical characteristic, each singly labeled microparticle being smaller than a resolution limit of said specific imaging system employed to optically distinguish said optically discriminable reporter; and

(b) combining a plurality of said singly labeled microparticles together to generate an aggregate reporter having a size that is still smaller than said resolution limit, the aggregate reporter being optically distinguished by said specific imaging system in response to an optical characteristic of the aggregate reporter other than size and shape.--

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314